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CLAIMS:

1. A method for the prophylaxis or treatment of infection by a protozoan parasite in an animal or bird, said method comprising administering to said animal or bird, ~~an nitric oxide~~ a nitric oxide (NO) modifying agent which kills, inhibits or otherwise retards the growth, infectivity or pathogenesis of said parasite.

2. A method for the prophylaxis or treatment of a disease condition caused or exacerbated by a protozoan parasite in an animal or bird, said method comprising administering to said animal or bird an NO modifying agent which kills, inhibits or otherwise retards the growth, infectivity or pathogenesis of said parasite such that the disease condition is ameliorated.

3. A method for the prophylaxis or treatment of infection by a protozoan parasite or a disease condition caused by a protozoan parasite in an animal or bird, said method comprising administering to said animal or bird an effective amount of an NO modifying agent for a time and under conditions sufficient to treat the infection and/or disease condition as determined by any one or more of the following parameters:

(i) inhibition, retardation or killing of any life cycle stages of said parasite;
(ii) inhibition, retardation or reduction in pathological adherence processes of parasitized host cells;
(iii) inhibition, retardation or reduction of the ability of various life cycle stages of the parasite to bind, ~~associate or otherwise adhere~~ to cells;
(iv) inhibition or suppression of parasite induced host production of one or more cytokines associated with pathogenesis of the disease;
(v) amelioration of clinical symptoms of the disease conditions;
(vi) amelioration of any ischaemia/reperfusion injury resulting from pathophysiological processes occurring in malaria or its treatment; and/or
(vii) replacement of deficiency of NO at systemic, organ or tissue levels or insufficient production occurring in the disease process caused by malaria.

4. ~~A method~~ The method according to claim 1 or 2 or 3 wherein the animal is a mammal.

5. ~~A method~~ The method according to claim 4 wherein the mammal is a human.

6. ~~A method~~ The method according to claim 1 or 2 or 3 wherein the protozoa is a species of *Plasmodium*.

7. ~~A method~~ The method according to claim 1 or 2 or 3 wherein the protozoa is *Plasmodium falciparum*.

8. ~~A method~~ The method according to claim 1 or 2 or 3 wherein NO is administered by inhalation to increase systemic NO levels or NO effect.

9. ~~A method~~ The method according to claim 1 or 2 or 3 wherein the agent is an NO donor.

10. ~~A method~~ The method according to claim 1 or 2 or 3 wherein the NO modifying agent is targeted to an organ or tissue associated with a particular life cycle stage of the parasite or particular pathology of the disease caused by the parasite.

11. A method according to ~~claim~~ 10 wherein the organ or tissue targeted is selected from the liver, brain, endothelial cells, macrophages/monocytes and red blood cells.

12. ~~A method~~ The method according to claim 11 wherein the organ or tissue targeted is the liver or brain.

13. A method according to claim 9 wherein the NO modifying agent results in the formation within the circulatory stem and/or tissues of NO in the form of a compound of formula:

R-NO

wherein R is an NO releasing, delivering or transferring moiety such as an amino acid, peptide,

polypeptide, protein, enzyme, amine, glycolipid, polysaccharide or a chemical derivative thereof.

14. The method ~~A method~~ according to claim 8 where the NO donor results in the formation of or is itself a R'-S-NO compound where the moiety R'-S- is derived from the corresponding thiol, R'-SH.

15. The method ~~A method~~ according to claim 8 or 9 wherein the R, R'-S- or R'-SH groups include or are derived from cysteinylglycine, cysteine, cysteamine, lipoic acid, dithiothreitol, glutathione, L-arginine, penicillamine, N-acetyl-penicillamine, N-acetylcysteine, albumin, tissue plasminogen activator, streptokinase, a cytokine or an antagonist or agonist of a cytokine (eg. an antibody to a cytokine or soluble receptor for a cytokine or a fragment of a cytokine or a cytokine binding protein) an interferon (IFN) such as IFNα, IFNβ, IFNγ, a growth factor such as granulocyte colony-stimulating factor (G-CSF), granulocyte-macrophage colony-stimulating factor (GM-CSF), an interleukin (IL) such as IL-1 to IL-13, haemoglobin and a cathepsin such as cathepsin B.

16. The method ~~A method~~ according to claim 1 wherein the agent comprises a combination of one of a nitrosothiol and another agent ~~the other an agent~~ selected from a cytokine and a chemotherapeutic agent.

17. A method for the prophylaxis or treatment of infection by a *Plasmodium* species in a mammal, said method comprising administering ~~administered~~ to said mammal an NO modifying agent which kills, inhibits or otherwise retards the growth, infectivity or pathogenesis of the *Plasmodium species*.

18. A method for the prophylaxis or treatment of a disease condition caused by or exacerbated by a protozoan parasite in a mammal, said method comprising administering to said mammal an NO modifying agent which kills, inhibits or otherwise retards the growth, infectivity or pathogenesis of said parasite such that the disease condition is ameliorated.

19. A method for the prophylaxis or treatment of infection by a *Plasmodium* species or a disease condition caused by a *Plasmodium* species in a mammal, said method comprising

administering to said mammal an effective amount of an NO modifying agent for a time and under conditions sufficient to treat the infection and/or disease condition as determined by any one or more of the following paramcters:

(i) inhibition, retardation or killing of any life cycle stages of said *Plasmodium* species;

(ii) inhibition, retardation or reduction in pathological adherence processes of host cells parasitized by said *Plasmodium* species;

(iii) inhibition, retardation or reduction of the ability of various life cycle stages of the *Plasmodium* species to bind, ~~associate or otherwise adhere~~ to cells such as but not limited to binding and invasion of hepatocytes and/or RBCs such as by sporozoites and merozoites, ~~respectively of their equivalents~~.

(iv) inhibition or suppression of *Plasmodium* species induced host production of one or more cytokines associated with pathogenesis of the disease;

(v) amelioration of clinical symptoms of the disease condition;

(vi) amelioration of any ischaemia/reperfusion injury resulting from pathophysiological processes occurring in malaria or its treatment; and/or

(vii) replacement of deficiency of NO at systemic, organ or tissue levels or insufficient production occurring in the disease process caused by malaria.

20. A method according to claim 17 or 18 or 19 wherein the *Plasmodium* species is *Plasmodium falciparum.*

21. The method ~~A method~~ according to claim 20 whercin the mammal is a human.

22. The method ~~A method~~ for the prophylaxis and treatment of malaria or another related disease condition caused by *Plasmodium* species in a mammal said method comprising administering to said mammal an NO modifying agent which kills, inhibits or otherwise retards the growth, or pathogenesis of said *Plasmodium* species.

23. A method for the prophylaxis or treatment of malaria or another related disease condition caused or exacerbated by *Plasmodium* species in a mammal, said method comprising

administering to said mammal an NO modifying agent which kills, inhibits or otherwise retards the growth, infectivity or pathogenesis of the *Plasmodium* species such that the malaria is ameliorated.

24. A method for the ~~prophylaxis of treatment~~ prophylaxis or treatment of infection by a *Plasmodium* species or a malarial disease condition caused by a *Plasmodium* species in a mammal, said method comprising administering to said mammal an effective amount of an NO modifying agent for a time and under conditions sufficient to treat the infection and/or malarial disease condition as determined by any one or more of the following parameters;

(i) inhibition, retardation or killing of any life cycle stages of said *Plasmodium* species, and in particular *P. falciparum;*

(ii) inhibition, retardation or reduction in pathological adherence processes of host cells parasitized by said *Plasmodium* species such as parastizied RBCs or parasitized hepatocytes;

(iii) inhibition, retardation or reduction of the ability of various life cycle stages of the *Plasmodium* species to bind, ~~associate or otherwise adhere~~ to cells such as but not limited to binding and invasion of hepatocytes and/or RBCs such as by sporozoites and merozoites, ~~respectively of their equivalents~~.

(iv) inhibition or suppression of *Plasmodium* species' induced host production of one or more cytokines associated with pathogenesis of the disease and in particular malaria;

(v) amelioration of clinical symptoms of the malaria;

(vi) amelioration of any ischaemia/reperfusion injury resulting from pathophysiological processes occurring in malaria or its treatment; and/or

(vii) replacement of deficiency of NO at systemic, organ or tissue levels or insufficient production occurring in the disease process caused by malaria.

25. ~~A method~~ The method according to claim 22 or 23 or 24 wherein the *Plasmodium* species is *P. falciparum*.

26. ~~A method~~ The method according to claim 22 or 23 or 24 wherein the mammal is a human.

27. An NO modifying agent which exhibits one or more of the following properties:

(i) inhibition, retardation or killing of any life cycle stages of a parasite;
(ii) inhibition, retardation or reduction in pathological adherence processes of parasitized host cells;
(iii) inhibition, retardation or reduction of the ability of various life cycle stages of the parasite to bind, associate or otherwise adhere to cells;
(iv) inhibition or suppression of parasite induced host production of one or more cytokines associated with pathogenesis of the disease;
(v) amelioration of clinical symptoms of the disease conditions;
(vi) amelioration of any ischaemia/reperfusion injury resulting from pathophysiological processes occurring in malaria or its treatment; and/or
(vii) replacement of deficiency of NO at systemic, organ or tissue levels or insufficient production occurring in the disease process caused by malaria.

28. An NO modifying agent which exhibits one or more of the following properties:

(i) inhibition, retardation or killing of any life cycle stages of a *Plasmodium* species;
(ii) inhibition, retardation or reduction in pathological adherence processes of host cells parasitized by a *Plasmodium* species;
(iii) inhibition, retardation or reduction of the ability of various life cycle stages of the *Plasmodium* species to bind, associate or otherwise adhere to cells such as but not limited to binding and invasion of hepatocytes and/or RBCs such as by sporozoites and merozoites, respectively or their equivalents;
(iv) inhibition or suppression of *Plasmodium* species induced host production of one or more cytokines associated with pathogenesis of the disease;
(v) amelioration of clinical symptoms of the disease condition;
(vi) amelioration of any ischaemia/reperfusion injury resulting from pathophysiological processes occurring in malaria or its treatment; and/or
(vii) replacement of deficiency of NO at systemic, organ or tissue levels or insufficient production occurring in the disease process caused by malaria.

29. An NO modifying agent which exhibits one or more of the following properties:

(i) inhibition, retardation or killing of any life cycle stages of *Plasmodium* species, and in particular *P. falciparum;*

(ii) inhibition, retardation or reduction in pathological adherence processes of host cells parasitized by said *Plasmodium* species such as parastizied RBCs or parasitized hepatocytes;

(iii) inhibition, retardation or reduction of the ability of various life cycle stages of the *Plasmodium* species to bind, associate or otherwise adhere to cells such as but not limited to binding and invasion of hepatocytes and/or RBCs such as by sporozoites and merozoites, respectively of their equivalents.

(iv) inhibition or suppression of *Plasmodium* species' induced host production of one or more cytokines associated with pathogenesis of the disease and in particular malaria; and/or

(v) amelioration of clinical symptoms of the malaria.

30 A composition containing an agent according to claim 27 or 28 or 29 and one or more pharmaceutically acceptable carriers and/or diluents.

31 A method of determining a predisposition to clinical or severe malaria said method comprising genetically determining a polymorphism in a gene for NO synthase or a cytokine capable of influencing NO levels.

32 A method of determining which patients with clinical or severe malaria will benefit from the administration of NO modifying therapy said method comprising determining genotype of cytokine genes or NO synthase gene.

33 A method according to claim 31 or 32 the presence of a polymorphism in the NOS2 gene, γ-IFN gene, IL-12 gene or α-IFN gene.

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